

CLAIMS

WHAT IS CLAIMED IS:

1. A method of examining the physiological effect of a compound on a mammalian prostate cancer cell wherein said prostate cancer cell expresses an exogenous wild type androgen receptor polynucleotide that encodes an androgen receptor polypeptide or an androgen receptor polypeptide variant, said cell further comprising an abnormal level of mRNA that encodes said androgen receptor polypeptide or said androgen receptor polypeptide variant when compared to the level of mRNA that encodes said androgen receptor polypeptide or said androgen receptor polypeptide variant in a normal prostate cell, said method comprising:
 - (a) determining that said abnormal level of mRNA in said prostate cancer cell is at least two fold higher than the level of mRNA in said normal prostate cell;
 - (b) contacting a compound to be tested with said prostate cancer cell to provide a treated prostate cancer cell; and
 - (c) examining one or more physiological characteristics of said treated prostate cancer cell.

2. A method of examining the physiological effect of a compound on a mammalian prostate cancer cell wherein said prostate cancer cell expresses an exogenous wild type androgen receptor polynucleotide that encodes an abnormal level of androgen receptor polypeptide or an abnormal level of androgen receptor polypeptide variant when compared to the level of androgen receptor polypeptide or androgen receptor polypeptide variant encoded by a normal prostate cell, said method comprising:
 - (a) determining that said abnormal level of androgen receptor polypeptide or said abnormal level of androgen receptor polypeptide variant is at least two fold higher than the level of androgen receptor polypeptide or androgen receptor polypeptide variant in said normal prostate cell;
 - (b) contacting a compound to be tested with said prostate cancer cell to provide a treated prostate cancer cell; and

(c) examining one or more physiological characteristics of said treated prostate cancer cell.

3. A method of examining the physiological effect of a compound on a mammalian prostate cancer cell according to claim 1 which includes the additional steps of:

(a) providing a mammalian prostate cancer cell which is the same as said prostate cancer cell and which is not contacted with said compound to thereby provide a control prostate cancer cell;

examining said one or more physiological characteristics of said control prostate cancer cell; and

comparing said one or more characteristics of said control prostate cancer cell with said one or more characteristics of said treated prostate cancer cell.

4. A method of examining the physiological effect of a compound on a mammalian prostate cancer cell according to claim 2 which includes the additional steps of:

(a) providing a mammalian prostate cancer cell which is the same as said prostate cancer cell and which is not contacted with said compound to thereby provide a control prostate cancer cell;

examining said one or more physiological characteristics of said control prostate cancer cell; and

comparing said one or more characteristics of said control prostate cancer cell with said one or more characteristics of said treated prostate cancer cell.

5. A method of examining the physiological effect of a compound on a selected mammalian cancer cell wherein said cancer cell expresses an exogenous wild type polynucleotide that encodes a protein or polypeptide of interest, said cell further comprising an abnormal level of mRNA that encodes said protein or polypeptide of interest when compared to the level of mRNA that encodes said protein or polypeptide of interest in said normal selected cell, said method comprising:

- (a) determining that said abnormal level of mRNA in said selected cancer cell is at least two fold higher than the level of mRNA in said normal selected cell;
- (b) contacting a compound to be tested with said selected cancer cell to provide a treated cancer cell; and
- (c) examining one or more physiological characteristics of said treated cancer cell.

6. A method of examining the physiological effect of a compound on a selected mammalian cancer cell wherein said selected cancer cell expresses an exogenous wild type polynucleotide that encodes an abnormal level of protein or polypeptide of interest when compared to the level of said protein or polypeptide of interest encoded by a normal selected cell, said method comprising:

- (a) determining that said abnormal level of said protein or polypeptide of interest is at least two fold higher than the level of said protein or polypeptide of interest in said normal selected cell;
- (b) contacting a compound to be tested with said selected cancer cell to provide a treated cancer cell; and
- (c) examining one or more physiological characteristics of said treated cancer cell.

7. A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 5 which includes the additional steps of:

- (a) providing a mammalian cancer cell which is the same as said selected cancer cell and which is not contacted with said compound to thereby provide a control cancer cell;
- examining said one or more physiological characteristics of said control cancer cell; and
- comparing said one or more characteristics of said control cancer cell with said one or more characteristics of said treated cancer cell.

8. A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 6 which includes the additional steps of:

(a) providing a mammalian cancer cell which is the same as said selected cancer cell and which is not contacted with said compound to thereby provide a control cancer cell;

examining said one or more physiological characteristics of said control cancer cell; and

~~comparing said one or more characteristics of said control cancer cell with said~~
one or more characteristics of said treated cancer cell.

9. A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 5 or 6 wherein said selected mammalian cell is selected from the group consisting of breast cancer cells, ovarian cancer cells and prostate cancer cells.

10. A method of inhibiting the growth of hormone refractory prostate cancer cells wherein said cells comprise androgen receptors that exhibit biological function, said method comprising the step of decreasing the biological function of said androgen receptors.

11. A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 10 wherein said step of decreasing the biological function of said androgen receptors comprises affecting the androgen receptor DNA levels, androgen mRNA levels, or androgen protein levels.

12. A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased through modulation of signal transduction pathways such as targeting EGF receptors that crosstalk to the androgen receptor.

13. A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased by the induction of cellular degradation pathways.

14. A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased by dissociating the androgen receptor from heat shock proteins that maintain the androgen receptor integrity.

15. A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased using androgen receptor antisense or mRNA knockdown technology.

17. A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein is decreased by modifying the polynucleotide or polypeptide sequence of the androgen receptor or by posttranslational modifications of the androgen receptor selected from the group consisting of phosphorylation, acetylation, ubiquitination, and sumolation.

18. A method for determining if a selected prostate cancer cell is hormone sensitive or has become hormone refractory, said method comprising the steps of:

- (a) determining the level of mRNA in said selected cell that encodes the androgen receptor polypeptide or androgen receptor polypeptide variant;
- (b) determining the level of mRNA in a hormone sensitive selected prostate cancer cell;
- (c) comparing the level of mRNA determined in step (a) to the level of mRNA determined in step (b); and
- (d) determining that the selected prostate cancer cell is hormone sensitive or has become hormone refractory if the level of mRNA determined in step (a) is at least two fold higher than the level of mRNA determined in step (b).

19. A method for determining if a selected prostate cancer cell is hormone sensitive or has become hormone refractory, said method comprising the steps of:

(a) determining the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant in said selected cell;

(b) determining the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant in a hormone sensitive selected prostate cancer cell;

(c) comparing the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (a) to the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (b); and

(d) determining that the selected prostate cancer cell is hormone sensitive or has become hormone refractory if the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (a) is at least two fold higher than the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (b).